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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/875,305	06/05/2001	Victor J. Dzau	50025/003003	7095

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EXAMINER
MARVICH, MARIA

ART UNIT	PAPER NUMBER
1636	14

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/875,305	DZAU ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This office action is in response to an amendment filed 12/10/02. Claims 13-27 are pending in this application.

Priority

It is noted that this application appears to claim subject matter disclosed in prior copending Application No. 08/524,206, filed 9/8/1995. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question

whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Response to Amendment

Objection to the Specification had been withdrawn in light of submission of figures in place of tables 5 and 6.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. For reasons given in the first office action and as discussed below, these claims are rejected.

Response to Arguments

Applicants traverse the claim rejection of claim 13-27 under 112, first paragraph, for lack of enablement on page 2-8 of the response filed 12/10/02. Applicant argues against the rejection that the specification does provide the evidence of the operability of the instant invention *in vivo*. Specifically, applicant cites the successful use of NFkB decoys for the treatment of ischemic

reperfusion injury, inflammatory arthritis, glomerulonephritis, cytokine production and tumor growth in rat animal models. Applicant argues that submission of human clinical trials is not a requirement for patentability of inventions directed to treatment of humans. As a demonstration that decoy therapy is a viable form of treatment of human disease, E2F decoy therapy and studies by Tomita et al. are cited. These primarily are used to demonstrate that the general mechanism of treatment with decoys is enabled. Specifically, applicant states that the examiner cited no reasons why the positive results obtained with decoys to one specific transcription factor would not be applicable to 1) the assessment of the viability of clinical strategy 2) mode of delivery and mode of operation of other transcription factors.

Applicant's arguments filed 12/10/02 have been fully considered but they are not persuasive. The instant application recites a method for ***preventing*** or treating an ***NFkB-associated disease or condition*** by introduction of an NFkB decoy. Applicant points to the specification and to E2F decoy PREVENT and to Tomita et al. as to the suitability of NFkB decoy therapy in humans. As the specification teaches only that the specific mode of treatment for NFkB decoys is introduction of such as a polymer or liposomes (table page 11), applicant argues that examples 2 and 3 of the specification, E2F decoy use in rats is demonstrated, and clinical data performed post filing demonstrate the suitability of decoy therapy. While these teachings provide guidance with regard to treatment of patients suffering from vein graft failure, there is no guidance for treatment of NFkB associated diseases and conditions with NFkB decoys. The teaching of the specification and prior art do not teach one how to make or use NFkB decoys for therapeutic purposes as neither the specification nor the prior art provide the specific dosages to be administered to patients, the schedule of treatments, the specific modes of

administration, the intended therapeutic targets or organs for NFkB decoy therapy. Finally, neither the specification nor the prior art recognizes any set of diseases as being an NFkB associated diseases or conditions. Therefore, without guidance as to what criteria or guidance are to be used to define and identify NFkB-associated diseases and conditions, the metes and bounds of the claimed diseases cannot be determined and the recited the diseases are unknown. Therefore, the sites of administration, the intended therapeutic product and the intended target organs are unknown. Disease prevention is highly unpredictable as it is unclear for whom the treatment is targeted.

The aim of the Tomita studies was to transfect cells with an NFkB decoy. The applicants argue that the studies rely upon the previously reported work with E2F for its methods. The method that the NFkB study does share is for the preparation of the HVJ liposomes. This is a general mechanism for delivery of substances to cells. However, as the E2F decoy studies were performed *in vivo* on rat models for vein bypass studies, little support for NFkB decoy therapy can be derived from the E2F data such as decoy target organs, means of inducing the diseased state in the animal model, means of administration of the decoy, decoy dosages and schedule of treatment and means of assaying treatment. Furthermore, the teachings of Tomita et al. do not suggest that their results in animals are predictive of the results that would be expected in humans. Therefore, it is not clear that reliance on the experimental models accurately reflects the relative efficacy of the claimed therapeutic strategy.

The argument that absolute predictability of success in human therapy is not a requirement for patentability and specifically for enablement is not germane, as clinical trials were not requested as evidence that NFkB decoy therapy is enabled.

Claims 13-27 remain rejected under 112, first paragraph due to the lack of direction or guidance presented, the absence of working examples and the unpredictable and undeveloped state of the art. Therefore, the skilled artisan attempting to practice methods of treatment and prevention of NFkB –associated diseases with NFkB decoys would have needed to practice undue and excessive experimentation.

Claim rejections under 112, first paragraph, for lack of written description have been withdrawn In light of applicant's remarks. NFkB is a well-known transcription factor and the binding sequences for NFkB are equally well documented.

Conclusion

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3291.

Maria B Marvich, PhD
Examiner
Art Unit 1636

February 24, 2003